REMARKS

Claims 19, 41, 43 and 44 have been amended. Claim 42 has been cancelled. No new matter has been added. Thus, claims 19-36, 41, 43, 44 and 49-58 are pending.

Claim Objections

The objections to claims 42-44 have been obviated by appropriate amendment. Claim 42, which was objected to as a substantial duplicate of claim 41, has been cancelled. Claims 43 and 44, which were objected to as depending on non-elected claims 2 and 8, have been amended. Amended claims 43 and 44 now depend on elected claim 41 and have been amended to make them consistent with claims 43 and 44 as originally filed.

Rejections under 35 U.S.C. § 112

Claims 19-36, 41-44 and 49-58 were rejected under 35 U.S.C. § 112, 2nd paragraph as being indefinite. The rejection of the claims under 35 U.S.C. § 112 has been obviated by appropriate amendment. In line 4 of claim 19 and in line 2 of claim 41, the word "and" has been replaced with the word --or--. In addition, the spelling of "enantiomers" in claim 41 has been corrected. In view of these amendments, Applicants assert that all of the presently presented claims fully meet the requirements of 35 U.S.C. § 112, 2nd paragraph and request that these rejections be withdrawn.

Rejections under 35 U.S.C. § 102

Rejection over Luk et al.

Claims 19-36, 41-44 and 49-58 were rejected under 35 U.S.C. § 102(a) over Luk et al. (*Langmuir* **2000**, *16* (24), 9604-9608). In the alternative, the claims were rejected under 35 U.S.C. § 103(a) as obvious over Luk et al.. The rejection of the claims over Luk et al. is respectfully traversed. Applicants point out that the earliest publication date of this reference was October 21, 2000, which is after the filing date of the present application (October 11, 2000). This publication date is noted on the bottom of page 9604 of the reference in the statement "Published on Web 10/21/2000." Accordingly,

Luk et al. is **not** a proper reference under 35 U.S.C. § 102(a). Applicants apologize for any confusion that may have resulted from the incorrect listing of the publication date of this reference in the First Supplemental Information Disclosure Statement and PTO FORM 1449 filed on September 23, 2002.

Rejection over Chapman et al.

Claims 19, 29, 31, 36 and 41 were rejected under 35 U.S.C. § 102(a) over Chapman et al. (*J. Am. Chem. Soc.* **2000**, *122* (34), 8303-8304). In the alternative, the claims were rejected under 35 U.S.C. § 103(a) as obvious over Chapman et al.. The rejection of the claims over Chapman et al. is respectfully traversed. In the attached Declaration Pursuant to 37 CFR 1.131, the declarant, inventor Milan Mrksich, states that he and the co-inventor had completed the invention described and claimed in the present application prior to August 12, 2000, the earliest publication date of Chapman et al.. Accordingly, Chapman et al. is **not** a proper reference under 35 U.S.C. § 102(a).

Rejections under 35 U.S.C. § 103

Rejection over Mrksich et al., Hodneland et al. (I), Houseman et al., Sigal et al., Deng et al., and Hodneland et al. (II)

Claims 29, 36, 57 and 58 were rejected under 35 U.S.C. § 103(a) over Mrksich et al., in view of Hodneland et al. (I), Houseman et al. and Sigal et al., and further in view of Deng et al. and Hodneland et al. (II), with reference to the reasoning set forth in the previous Office Action (April 23, 2002; paper no. 8). In response to Applicants' arguments in the Amendment And Reply filed on September 23, 2002, the Office Action points out that claims 29, 36, 57 and 58 do not require a "-T" group as recited in claims 19 and 41. The Office Action asserts that it would be obvious to select alkanethiol or alkanethiolate moieities as described in Mrksich et al. in view of the groups disclosed by the secondary references to provide a monolayer that would inherently meet the cell patterning test recitation of independent claim 29.

Independent claim 29 is directed to a substrate comprising a monolayer, and recites that the monolayer comprising alkanethiolate moieties "does not fail a cell

patterning test at 12 days." Claims 36, 57 and 58 depend from claim 29. The "cell patterning test" referred to in claim 29 is described in the specification on page 12, lines 1-16. This test can be used to measure inertness of surfaces, including surfaces having monolayers comprising alkanthiolate moieties. It is further noted in this section of the specification that monolayers containing alkanthiolate moieties of the present invention do not fail the cell patterning test for at least 12 days (p.12, lines 14-16). In contrast, alkanethiolate moieties terminated in tri(ethylene glycol) moieties are described as failing the cell patterning test in 7 days. Comparative data presented in the specification show that monolayers of tri(ethylene glycol)-terminated alkanethiolates fail the cell patterning test within one week, whereas monolayers of the present invention do not fail for at least two weeks or for at least three weeks (p. 18, line 25 through p. 19, line 21). Thus, monolayers of the present invention can extend the time course over which cells can be patterned in culture and can extend the times over which cultured cells can be maintained in patterns (p.23, lines 19-27).

The rejection of the claims under 35 U.S.C. § 103(a) over Mrksich et al., Hodneland et al. (I), Houseman et al., Sigal et al., Deng et al., and Hodneland et al. (II) is respectfully traversed. The cited references, alone or in combination do not teach or suggest each and every element of the claims. Specifically, the references do not teach or suggest a monolayer comprising alkanethiolate moieties where the monolayer does not fail a cell patterning test at 12 days.

Mrksich et al. ("A18"; *Am. Chem. Soc. Symp. Ser.* **1997**, *680*, 361-373) discloses inert monolayers containing alkanethiolates terminated only in oligo(ethylene glycol) moieties (p. 361) and/or in tri(propylene sulfoxide) moieties (p. 365). The tri(propylene sulfoxide)-containing alkanethiolates are described as "similarly effective at resisting adsorption" relative to the oligo(ethylene glycol)-containing alkanethiolates (p.365, lines 13-15). Thus, Mrksich et al. discloses only alkanethiolates containing oligo(ethylene oxide) moieties or alkanethiolates having similar levels of inertness. The inert properties of these monolayers are confirmed by the disclosure of the secondary reference Deng et al. ("A3"; *J. Am. Chem. Soc.* **1996**, *118* (21), 5136-5137), which states that monolayers of tri(propylene sulfoxide)-containing alkanethiolates permitted cell spreading after 1-2 days, whereas monolayers of oligo(ethylene oxide)-containing

alkanethiolates permitted cell spreading after 5-7 days (p. 5137, left column, lines 13-23). Thus, Mrksich et al. and Deng et al. disclose monolayers that fail a cell patterning test within at most 7 days.

Hodneland et al. (I) ("A7"; *J. Am. Chem. Soc.* **2000**, *122* (17), 4235-4236) discloses an inert monolayer of alkanethiolates terminated in a tri(ethylene glycol) moiety (Figure 1 and footnote 12). Likewise, Houseman et al. ("A9"; *Angew. Chem. Int. Ed.* **1999**, *38* (6), 782-785) discloses an inert monolayer of alkanethiolates terminated in a tri(ethylene glycol) moiety (Figure 1). Thus, Hodneland et al. (I) and Houseman et al. disclose only the tri(ethylene glycol)-containing alkanethiolate monolayers as described in Applicants' specification, which fail a cell patterning test in 7 days.

Sigal et al. ("A25"; *J. Am. Chem. Soc.* **1998**, *120* (14), 3464-3473) presents inert monolayers of alkanethiolates terminated in a variety of moieties. The only monolayer that is presented as being sufficiently inert so as to resist adsorption of both small and large proteins is the monolayer containing alkanethiolates terminated in an oligo(ethylene glycol) moiety (Abstract, lines 10-14; p. 3472, right column, paragraph (iv)). The alkanethiolates compared in the disclosure of Sigal et al. include alkanethiolates derived from $HS-(CH_2)_{11}-OH$. These single-alcohol terminated alkanethiolates are identical to those described as providing an inert surface monolayer in Hodneland et al. (II) ("A8"; *Langmuir* **1997**, *13* (23), 6001-6003). Thus, Sigal et al. and Hodneland et al. (II) disclose monolayers that are no more inert than those provided by alkanethiolates terminated in oligo(ethylene glycol) moieties.

All of the references cited in this rejection, alone or in combination, teach that the optimum inertness of a monolayer of alkanethiolates is provided by alkanethiolates containing terminal oligo(ethylene glycol) moieties. This optimum intertness can only provide monolayers that fail a cell patterning test within 7 days. As described in Applicants' specification, the inertness of alkanethiolates containing tri(ethylene glycol) moieties (an oligo(ethylene glycol) moiety) is not sufficient to provide a monolayer that fails a cell patterning test at 12 or more days. There is thus no teaching or suggestion in any of these references, either alone or in combination, of a monolayer of alkanethiolates that fails a cell patterning test in 12 or more days. Contrary to the

assertion of the Office Action, the references do not teach or suggest "preferred groups" that can be selected to provide a monolayer that meets the cell patterning test recitation of claim 29. Accordingly, claims 29, 36, 57 and 58 are not obvious over the cited references, alone or in combination.

Rejection over Mrksich et al., Hodneland et al. (I), Houseman et al., Sigal et al., Luk et al., and Chapman et al.

Claims 19-36, 41-44 and 49-58 were rejected under 35 U.S.C. § 103(a) over Mrksich et al., Hodneland et al. (I), Houseman et al. or Sigal et al., in view of Luk et al. or Chapman et al. This rejection of the claims under 35 U.S.C. § 103(a) is respectfully traversed. The inapplicability of Luk et al. and Chapman et al. as references against the pending claims has been addressed above. As noted in the arguments above, Mrksich et al., Hodneland et al. (I), Houseman et al. and Sigal et al., alone or in combination, do not teach or suggest each and every element of claims 29, 36, 57 and 58. It is also apparent that Applicants' arguments in the Amendment And Reply filed on September 23, 2002 have eliminated these four references with respect to claims 19-28, 30-35, 41, 43, 44 and 49-56. Accordingly the references, alone or in combination, are insufficient to provide a *prima facie* of obviousness against pending claims 19-36, 41, 43, 44 and 49-58.

Double Patenting Rejection

Claims 19-36, 41-44 and 49-58 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-117 of U.S. Patent Application Serial No. 09/923,760 or claims 1-41 of U.S. Patent Application Serial No. 09/797,166, in view of Luk et al. or Chapman et al. The rejection of the claims under the judicially created doctrine of obviousness-type double patenting is respectfully traversed. The inapplicability of Luk et al. and Chapman et al. as references against the pending claims has been addressed above. It is apparent that Applicants' arguments in the Amendment And Reply filed on September 23, 2002 have eliminated the provisional rejection with respect to the co-pending U.S. Patent Applications alone. Accordingly,

there is insufficient evidence to provide a *prima facie* of obviousness-type double patenting against pending claims 19-36, 41, 43, 44 and 49-58.

Conclusion

In conclusion, all of the grounds raised in the outstanding Office Action for rejecting the application are believed to be overcome or rendered moot based on the amendments and remarks above. Thus, it is respectfully submitted that all of the presently presented claims are in condition for allowance. Should the Examiner feel a discussion would expedite the prosecution of this application, the Examiner is kindly invited to contact the undersigned.

Also submitted at this time is a Petition For Extension Of Time for one (1) month.

Respectfully submitted,

5/13/03

Jonathan P. Taylor, Ph.D.
Registration No. 48,338
Agent for Applicant

BRINKS HOFER GILSON & LIONE
P.O. BOX 10395
CHICAGO, ILLINOIS 60610
(312) 321-4200